III. REMARKS

Claim Status

Claims 1, 2, 5-12 and 14-22 are presently pending in the instant application. Claims 1, 6, 9, 16 and 21 have been amended. Claims 8, 12, and 14-15 have been cancelled

Applicants elected (4/01/2003) the chimeric oligonucleotide described by SEQ ID NO: 16. The remaining sequences have been cancelled from the claims.

Claim Rejections - 35 USC § 112 second paragrpah

Claims 1, 2, 5-12 and 14-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As pointed out by the examiner, claim 1, and those claims dependent therefrom, were amended to recite structures comprising a "P" moiety in the phosphorous linkage and outside the repeating units in each formula and have also used "P" to define the repeating unit since the term "P" is also used to define a phosphorous atom. As understood by the examiner, claim 1 goes on to define the term "p" in the claim, however the lower case "p" is not found in any of the structures.

Applicant apologizes for the lack of clarity in the amended claims. The "p" appearing outside the structure itself was intended as a lower case "p" but this was not clear from the structre drawings. Applicant has now renamed "p" to "z" to clarify the meaning.

Claim 9 recites "the oligonucleotides of claim 1, bound to telomerase..." This claim stands rejected as lacking antecedent basis for this limitation since the scope of claim 1 is limited to chimeric oligonucleotides. The examiner states that there is no support in claim 1 for the oligonucleotide further comprising a bound telomerase or wherein the bound telomerase is in a cell as recited in claims 10-11 and 17.

Applicant respectfully traverses this ground for rejection. Although claim 1 encompasses the oligonucleotide in its unbound state, it is properly limited by a claim directed to the oligonucleotide being bound to a specified moiety, in this case, telomerase. Basis for the bound oligo appears in the specification at pages 6 and 8.

Claims 14-15 stands rejected as being dependent upon a cancelled claim.

Applicant has cancelled these claims.

Claim 21 stands rejected for failing to identify the independent claim form which it depends.

Applicant has modified the claim reference thus obviating this ground for rejection.

Claim Rejections - 35 USC § 112 second paragraph

Claims 8, 12, and 14-15 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using chimeric oligonucleotides according to the present invention to inhibit telomerase activity *in vitro* comprising the administration of chimeric oligonucleotides, and

provides guidance for inhibiting telomerase activity in human cancer cells transplanted into a nude mouse, does not reasonably provide enablement for using chimeric oligonucleotides of undefined structure and/or target, *in vivo* for treating cancer in all non-human mammals.

Applicants have cancelled these claims.

Claim Rejections - 35 USC § 103

Claims 1-2, 5, 7, 9-11, 17-20, and 22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Uhlmann et al. in view of Norton et al. (1996) and Mata et al.

Uhlmann et al. teach the synthesis and properties of PNA and DNA chimeras of any desired sequence by an automated synthesizer and in one particular embodiment, disclose compounds of the following structure:

5'-GGGACCAtggcagcc-h where h is HN-$(CH_2)_6$-OH

which corresponds to nucleotides having oligomers on the 3' end of the structure comprising a terminal amino group having an acid labile protecting group.

However, as recognized by the examiner, Uhlmann et al. does not teach wherein n is at least 10 and not more than 20, and p is at least 3 and not more than 17. Moreover, Uhlmann et at. does not teach wherein this structure inhibits the activity of telomerase, or wherein the chimeric oligonucleotide structure comprises a terminal amino group.

Norton et al. is cited by the examiner as teaching the inhibition of human telomerase activity by peptide nucleic acids (PNAs). According to Norton et al. PNAs recognize the RNA component of human telomerase (hTR) and inhibit activity of the enzyme. Inhibition depends on targeting exact functional boundaries of the hTR template. Norton et al. also observed that phosphorothioate (PS) oligomers inhibit telomerase in a non-sequence selective fashion.

Additionally, Mata et al. is cited by the examiner as teaching that hexameric phosphorothioate oligomers function to inhibit telomerase activity and arrests growth of Burkitts lymphoma cells.

It is noted that the combination of references do not teach that n is at least 10 and not more than 20, and p is at least 3 and not more than 17.

The examiner concludes that it would have been obvious to the ordinary skilled artisan to combine the teachings of the above-cited references in the design of the present invention and that one of ordinary skill in the art would have been motivated to make the oligomers of the present invention to comprise wherein n is at least 10 and not more than 20, and p is at least 3 and not more than 17, since Uhlmann et al. clearly teach that chimeric PNA/DNA oligonucleotides or any sequence can be readily prepared.

The examiner also states that Norton et al. discloses the nucleotide structure of an oligomer 15 base pairs in length. Applicant has reviewed the Norton abstract cited by the examiner and respectfully, is unable to find reference in Norton to an

oligomer 15 base pairs in length. Furthermore, even if the reference did have such disclosure, it would not lead one skilled in the art to an appreciation of the number of units of "n" and the number of units of "p" [now "z"] that are the crux of applicant's invention.

With regard to the failure of the references to disclose the presence of a terminal primary amino group in the PNA oligomeric chimeras, the examiner states that the terminal secondary amino group in the compounds of Uhlmann et al. can readily be converted to a primary amino group. This may well be but the reference does not disclose such step, nor does it indicate the importance of such cleavage to a primary amine.

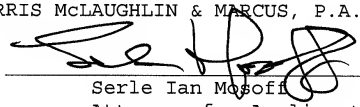
So all that is disclosed is a different composition that may by chemical manipulation be changed into the claimed compound, but without any understanding or motivation as to the benefit of the manipulation step.

Conclusion

Based on the foregoing remarks it is believed that the claim is in condition for allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved. If any extension of time for this response is required, Applicants request that this be considered a petition therefore. Please charge any insufficiency of fees, or credit any excess to Deposit Account No. 14-1263.

Respectfully submitted,

NORRIS McLAUGHLIN & MARCUS, P.A.

By 

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